Association of Leukaemia and Blood Groups

ROBERT SHIRLEY and R. G. DESAI*

From the Department of Medicine, Stanford University School of Medicine, Palo Alto, California, U.S.A.

During the past decade there has been increased interest in research on the association of ABO blood groups and diseases. Significant results have been obtained in patients with duodenal ulcer (Clarke, 1961), gastric cancer (Roberts, 1957), pernicious anaemia (*Brit. med. J.*, 1956), diabetes mellitus (Roberts, 1957), pituitary adenoma (Mayr, Diamond, Levine, and Mayr, 1956), and broncho-pneumonia in children (Struthers, 1951). Several other diseases have been investigated for such associations with statistically negative results (Roberts, 1957). The purpose of this report is to review what is known about the relation of ABO blood groups and leukaemia, acute and chronic, and to evaluate the data by the statistical method of Woolf (1955).

Methods

Several reports on leukaemia and ABO blood groups are recorded in the Table and analysed for the relative incidence of blood group A to blood group O by the method of Woolf. The latter, as explained in the original paper (Woolf, 1955), has the advantage of analysing heterogeneous material from populations of widely differing blood group incidences. In some of the reports reviewed, cases of acute leukaemia were classified according to cell type, but we have omitted such classifications and considered them all as acute leukaemia.

In addition to these published reports, we have included 177 cases of acute leukaemia studied by Dr. Henry Kaplan of this institution and added here with his permission. A total of 4360 cases of leukaemia were gathered; 2145 of these were acute, 1847 were chronic, and 368 were combined types, as obtained from 16 different world centres. Benda and Menghini (1957) and C. M. Baratta (1961, personal communication) did not separate their cases into acute or chronic variety. The statistical analysis of the data is as follows:

Acute Leukaemia. $X = 1 \cdot 12$ (relative incidence of A : O).
The χ^2 value for the difference between X and unity

is $4 \cdot 69$ and p value $0 \cdot 05$. The 95% confidence interval for the relative incidence of A : O is $- 1 \cdot 01, 1 \cdot 23$.
The χ^2 value of $4 \cdot 14$ for the heterogeneity of the areas is non-significant.

Chronic Leukaemia. $X = 1 \cdot 08$ (relative incidence of A : O).
The χ^2 value for the difference between X and unity is $1 \cdot 86$, which is not significant at the 5% level. The 95% confidence interval is $- 0 \cdot 97, 1 \cdot 20$.
The χ^2 value of $11 \cdot 38$ for heterogeneity is non-significant at the 5% level.

Total Leukaemia. In applying Woolf's method to the combined data the weighting technique must be slightly modified to take account of four control sets being identical for both acute and chronic leukaemia.
With this modification, $X = 1 \cdot 11$ (relative incidence of A : O).
The χ^2 value for the difference between X and unity is $8 \cdot 35$, which is significant with p value $0 \cdot 01$. The 99% confidence interval is $- 0 \cdot 01, 1 \cdot 22$.
The χ^2 value of $13 \cdot 13$ for heterogeneity is non-significant.
For the combined data the analysis by Woolf's technique is, in fact, somewhat unnecessary since in 13 out of the 16 cases the relative incidence of A : O is greater than one, which is significant at the 1% level by a simple, non-parametric combination of sign and rank permutation tests.

Discussion

The results indicate that there is a correlation between the incidence of blood group A and leukaemia. The difference, however, is slight, being only about 11%. This may explain the apparently negative results in the previously published articles where the number of cases never exceeded 750. The material for blood groups B and AB was not analysed because of the small samples involved.

It must, however, be noted that most of the published material on blood groups and leukaemia consists of brief summaries wherein the blood group data are frequently an incidental part of an article. Other investigators (Steinberg, 1960; Mustacchi, Shoenfeld, and Lucia, 1960; Buck-

TABLE
ABO BLOOD GROUPS AND LEUKAEMIA

Area	Author	Leukaemia					Control					R.I.* A:O
		O	A	B	AB	Total Number	O	A	B	AB	Total Number	
Acute Leukaemia												
Boston	Steinberg (1960) (9)	203 (45·1)	181 (40·2)	49 (10·9)	17 (3·8)	450 (100)	972 (44·3)	879 (40)	255 (11·6)	88 (4·1)	2194 (100)	0·986
Brooklyn	MacMahon and Folusiak (1958) (10)	280 (42·7)	246 (37·6)	101 (15·4)	28 (4·3)	655 (100)	900 (45·7)	728 (37)	261 (13·3)	78 (4)	1967 (100)	1·086
San Francisco	Lucia et al. (1958) (11)	58 (42·3)	60 (43·8)	17 (12·4)	2 (1·5)	137 (100)	2329 (45)	2070 (40)	569 (11)	207 (4)	5175 (100)	1·164
Mayo Clinic	Tinney and Watkins (1941) (12)	32 (41)	33 (42·4)	10 (12·8)	3 (3·8)	78 (100)	450 (45)	430 (43)	80 (8)	40 (4)	1000 (100)	1·079
San Francisco	H. Kaplan (1961) personal communication (18)	84 (47·4)	68 (38·4)	21 (11·9)	4 (2·3)	177 (100)	9473 (47·2)	7647 (38·1)	2127 (10·6)	823 (4·1)	20,070 (100)	1·003
New York, Maryland, San Francisco	Mustacchi et al. (1960) (13)	233 (40·9)	239 (41·9)	69 (12·1)	29 (5·1)	570 (100)	4560 (45·6)	3640 (36·4)	1350 (13·5)	450 (4·5)	10,000 (100)	1·255
Pavia, Italy	Ninni and Bedarida (1958) (14)	35 (44·8)	39 (50)	2 (2·6)	2 (2·6)	78 (100)	276 (43·1)	281 (43·9)	56 (8·8)	27 (4·2)	640 (100)	1·093
Chronic Leukaemia												
Chicago	Best et al. (1949) (15)	29 (35·8)	31 (38·3)	10 (12·3)	11 (13·6)	81 (100)	1985 (44)	1737 (38·6)	594 (13·2)	189 (4·2)	4505 (100)	1·222
Iowa City	Buckwalter et al. (1956) (16)	226 (49·5)	179 (39·3)	40 (8·8)	11 (2·4)	456 (100)	2892 (45·8)	2625 (41·6)	570 (9)	226 (3·6)	6313 (100)	0·873
Brooklyn	MacMahon and Folusiak (1958) (10)	281 (38·4)	273 (37·3)	122 (16·7)	56 (7·6)	732 (100)	900 (45·7)	728 (37)	261 (13·3)	78 (4)	1967 (100)	1·236
San Francisco	Lucia et al. (1958) (11)	93 (43·3)	96 (44·6)	17 (7·9)	9 (4·2)	215 (100)	2329 (45)	2070 (40)	569 (11)	207 (4)	5175 (100)	1·161
Mayo Clinic	Tinney and Watkins (1941) (12)	84 (46·7)	67 (37·2)	21 (11·7)	8 (4·4)	180 (100)	450 (45)	430 (43)	80 (8)	40 (4)	1000 (100)	0·873
Southern England	Kay and Shorter (1956) (17)	35 (40·7)	40 (46·5)	8 (9·3)	3 (3·5)	86 (100)	48,162 (45·2)	45,956 (43·2)	9059 (8·5)	3298 (3·1)	106,475 (100)	1·198
Pavia, Italy	Ninni and Bedarida (1958) (14)	31 (32)	50 (51·5)	11 (11·3)	5 (5·2)	97 (100)	276 (43·1)	281 (43·9)	56 (8·8)	27 (4·2)	640 (100)	1·584
Acute and Chronic Pooled												
Perugia, Italy	Benda and Menghini (1957) (7)	98 (38·4)	130 (51)	20 (7·9)	7 (2·7)	255 (100)	3163 (43)	3127 (42·5)	783 (10·6)	283 (3·9)	7356 (100)	1·342
Lima, Peru	C. M. Baratta (1961) personal communication (8)	70 (61·9)	28 (24·8)	13 (11·5)	2 (1·8)	113 (100)	66,706 (61·8)	25,797 (23·9)	12,413 (11·5)	3022 (2·8)	107,928 (100)	1·034

*Relative incidence of A:O blood groups.

walter, Wohlwend, Colter, Tidrick, and Knowler, 1956; Lucia, Hunt, and Petrakis, 1958; Tinney and Watkins, 1941; C. M. Barrata, 1961, personal communication; Best, Limarzi, and Poncher, 1949; Kay and Shorter, 1956) have also investigated blood groups and leukaemia associated with proper controls. It is evident from the above analysis that there is no statistical relation between specific type of leukaemia and blood groups, namely acute or chronic leukaemia. However, the total leukaemic data show some significant relation to blood type A (total leukaemia p value 0·01).

Although confirmation of these results must await further research, the data here should be of interest to those doing work on blood groups and diseases.

Summary

A statistical analysis of the relation of acute and chronic leukaemia to the incidence of A and O blood groups is presented, and 4360 cases reported from 16 different centres are analysed. There is no statistical relation between acute, chronic leukaemia and blood type. However, when the leukaemia cases are considered as a whole, blood type A preponderance seems significant.

REFERENCES

Benda, N., and Menghini, G. (1957). Correlazioni tra gruppi sanguigni ed incidenza di alcune forme morbose. *Riforma méd.* **71**, 169.

Best, W. R., Limarzi, L. R., and Poncher, H. G. (1949). Distribution of blood types in the leucemias. *J. Lab. clin. Med.*, **34**, 1587.

Brit. med. J. (1956). An association between blood group A and pernicious anaemia; a collective series from a number of centres. **2**, 723.

Buckwalter, J., Wohlwend, E. B., Colter, D. C., Tidrick, R. T., and Knowler, L. A. (1956). ABO blood groups and disease. *J. Amer. med. Ass.*, **162**, 1210.

Clarke, C. A. (1961). Blood groups and disease. *Progr. med. Genet.*, **1**, 81.

Kay, H. E. M., and Shorter, R. G. (1956). Blood groups in leukaemia and the reticuloses. *Vox Sang. (Basel)*, **1**, 255.

Lucia, S. P., Hunt, M. L., and Petrakis, N. L. (1958). The leukemias in relation to age, sex, and blood groups. *ibid.*, **3**, 354.

Mayr, E., Diamond, L. K., Levine, R. P., and Mayr, M. (1956). Suspected correlation between blood-group frequency and pituitary adenomas. *Science*, **124**, 932.

MacMahon, B., and Folusiak, J. C. (1958). Leukemia and ABO blood group. *Amer. J. hum. Genet.*, **10**, 287.

Mustacchi, P., Shoenfeld, E. M., and Lucia, S. P. (1960). Survival in acute leukemia: the influence of blood groups, sex, and age at onset. *Ann. intern. Med.*, **52**, 1099.

Ninni, M., and Bedarida, G. (1958). Rilievi statistici sui rapporti tra gruppi sanguigni e malattie. *Bibl. haemat. (Basel)*, **10**, 159.

Roberts, J. A. F. (1957). Blood groups and susceptibility to disease: A review. *Brit. J. prev. soc. Med.*, **11**, 107.

Steinberg, A. G. (1960). The genetics of acute leukemia in children. *Cancer (Philad.)*, **13**, 985.

Struthers, D. (1951). ABO blood groups of infants and children dying in the west of Scotland (1949–1951). *Brit. J. soc. Med.*, **5**, 223.

Tinney, W. S., and Watkins, C. H. (1941). Blood groups and blood dyscrasias. *Proc. Mayo Clin.*, **16**, 613.

Woolf, B. (1955). On estimating the relation between blood group and disease. *Ann. hum. Genet.*, **19**, 251.